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Narcolepsy Genetics, Autoimmunity, and Proposed Gene Therapies

Special Issue on Narcolepsy Drug Treatments

L-Tyrosine and Narcolepsy

Stimulants, antidepressants, and protein block L-tyrosine's action in the brain, helping explain conflicting reports of its therapeutic value.

Introduction

This issue of *Narcolepsy ☞ Sleep Disorders* contains the second of a three-part review of narcolepsy treatments. Our last issue dealt with non-drug therapies. This one reviews drug treatments. Our next will discuss the uncertain future of genetic therapies.

Our lead article reviews the literature on L-tyrosine, currently the most controversial substance used to treat narcolepsy.

Conflicting Results

L-tyrosine is an amino acid that the body uses to make important brain chemicals, including dopamine and norepinephrine. L-tyrosine can be considered a "natural" substance insofar as it is manufactured by the body itself and is found in many foods. According to certain clinical reports, however, when taken in concentrated form L-tyrosine can have therapeutic effects that far exceed anything ever claimed for conventional stimulants, antidepressants, or similar anti-narcoleptic drugs. How credible are those reports?

Between 1988 and 1995 three clinical studies and one theoretical paper have discussed the therapeutic effects of L-tyrosine on narcolepsy. Three of those four reports, including one just made public, have made positive, even stunning, claims for L-tyrosine's therapeutic value. The fourth

report, currently the most influential, makes highly negative claims.

The First French Study (1988)

The first positive study was made by a group of French sleep physicians and researchers led by Jacques Mouret. Even today, the study by Mouret's group is the only long-term study of L-tyrosine and narcolepsy ever undertaken. The group's spectacular results were published in December, 1988, in the premier British medical journal, *The Lancet* (1988; 2[8626-7]: 1458-9).

After a two-week drug washout, eight initial patients in the 1988 French study were treated for two years or more with varying dosages of L-tyrosine. After adjustments for individual responses, initial dosages in the study averaged 100 mg/kg per day — about 7 grams/day for a 154-pound person.

Patients who had previously used stimulants or tricyclic antidepressants responded much more slowly to the L-tyrosine than patients who had never used those drugs. (This is a key point we'll return to later.) Nevertheless, within six months all eight initial patients — including those who had earlier used other drugs — were reportedly completely free of cataplexy, sleep attacks, sleep paralysis, hypnagogic hallucinations, nighttime sleep disturbances, and the depression that frequently accompanies narcolepsy.

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